Lysozyme Aggregation and Fibrillation Monitored by Dynamic Light Scattering

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— The aggregation of amyloidogenic proteins provides a rich phase space with significant biomedical implications, including a link with several age-related diseases. We employed dynamic light scattering to monitor the aggregation of lysozyme, a model protein, from a monomeric state until the formation of micron-sized fibrils. For an aqueous lysozyme solution buffered at pH 2, the auto-correlation function of the scattered light intensity was found to be well-fit by a single exponential function with decay time \( \tau = 1/(2Dq^2) = 0.25 \) ms, which corresponds to a mean hydrodynamic radius \( R_H \) of 2.2 nm, very likely generated by monomers. Ethanol (4% v/v final concentration) induced a partial unfolding, to \( R_H = 4.6 \) nm. The subsequent addition of 70 mM KCl was found to shrink the size back to \( R_H = 2.5 \) nm, as expected when a denatured protein refolds due to partial screening of the intramolecular repulsion. However, further aggregation was not observed. At pH 4, using a low-salt acetate buffer, more ethanol (10% v/v) was required to initiate unfolding, but once it occurred, larger aggregates formed. These results are consistent with the model that partial unfolding, which exposes beta-motif secondary structure, is a prerequisite for aggregation and fibrillation, but the aggregation fate depends on the protein charge state (pH) and screening (salt concentration).